The Study of Evolution in the Field of Blood Glucose Monitoring System

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Abstract— This paper proposes the study of evolution in the field of blood glucose monitoring. The first system was introduced in 1970 after that, significant developments in design and technology are done by many other scientist and engineers. This paper discusses those key factors that influenced this evolution and the challenges to improve the performance. Paper also describes the rise of optical based blood glucose monitoring system.

Keywords: Blood Glucose. Blood Glucose Monitoring System

I. INTRODUCTION

The Egyptians made the first mention of diabetes around 1500 BC. The Greek physician Aretaeus (130–200 CE) noted a disease with symptoms of constant thirst, excessive urination and loss of weight, and named the condition 'diabetes', meaning 'flowing through'. The first clear reference to diabetes was made by an Arab physician, Avicenna (980–1037 CE), who accurately described in detail the clinical features and complications of the disease and its progress.

It was not until the early 19th century that glucose was identified as the sugar present. This association was supported in 1838 when George Rees, a physician at Guy's Hospital in London isolated sugar in excess from the blood serum of a diabetic patient.[8]

Towards the end of the 19th century a quantitative blood sugar method was published which used copper reduction and gravimetric measurement.[11]Stanley Benedict devised an improved copper reagent for urine sugar in 1908, [12] and this became, with modifications, the mainstay of urine monitoring of diabetes for over 50 years.

It is over 40 years since Anton Clemens at the Ames Research Division, Miles Laboratories, in Elkhart, Indiana, USA, developed the first blood glucose meter. It combined dry chemistry test strips (Dextrostix) with reflectance photometry to measure blood glucose. The concept of dry chemistry would be elegantly developed later for the analysis of other analytes.[1] Consequently, the first blood glucose meters represent an important landmark technology, which influenced the extensive growth of point-of-care (POC) testing in the mid-1980s.[2] Great progress has been achieved in the development of blood glucose meters and this continues to be an active field of study and research.[3, 4]

A breakthrough in the treatment and improvement in the lives of diabetics came about in 1921 when Frederick G. Banting, his assistant, Charles Best, and J. R. Macleod succeeded in the identification of insulin, the pancreatic hormone deficient in diabetes, which was confirmed in human studies. Large-scale commercial extraction and purification of animal insulin led the way to the treatment for diabetes and to the development of improved testing systems.

II. FIRST BLOOD GLUCOSE METERS: 1970–1980

Interest in diabetes was intensified during the 1970s by the introduction of glycated hemoglobin (HbA1c) measurement as an index of the quality of glycaemic control, and a major trial of type 2 diabetes commenced in 1977 in the UK to study the effect of close control of blood glucose and he risk of clinical complications. However, many reports identified potential practical problems and emphasized the need to improve portability, ease of use, accuracy and precision that could be achieved by patient home-monitoring and to be able to act on the result to adjust their therapy. There were also concerns about the funding of meters, and liability in the event of errors.

Anton Clemens at Ames developed an instrument to produce quantitative blood glucose results with Dextrostixin the late 1960s, and the first model became available in 1970[8].He applied the key principle of using reflected light from the surface of the solid strip, which was captured by a photoelectric cell to produce a signal that was displayed by a moving pointer on three analogue scales, equivalent to 0–4, 4–10 and 10–55 mmol/L blood glucose.

In 1972 the Japanese company Kyoto-Daiichi (later Arkray) produced the Eyetone blood glucose meter and had a marketing agreement with Ames to launch the product in the USA. The Eyetone also used reflectance photometry and the Dextrostix reagent test strips. It had an AC adaptor to use mains power and a single analogue scale and two standard strips for calibration. As it used mains power, it was lighter and easier to operate then the ARM, and, more importantly, it was slightly cheaper. Generally, performance from a limited number of studies was considered acceptable, with good precision and correlation. [8, 9]

In 1974, Boehringer Mannheim produced the Reflomat, are flectance meter using a modified reagent strip, requiring a much smaller volume of blood (20–30 μL), which was removed more simply by wiping with a cotton wool ball. Up to now, the blood glucose meters available were designed for testing in doctors' offices and it was not until the mid-1970sthat the idea of diabetics self-testing was contemplated. [10, 11]

Fig. 1: Boehringer Mannheim introduced the Reflomat in 1974 and the Reflolux in 1984.

III. THE CHALLENGES: 1981–1990

The 1980s was an active phase in the evolution of meters, which were becoming easier to use, smaller in size, with more variation in design, often with software memory to store and retrieve results. Reagent strips were also changing to accept smaller volumes of blood, and some were barcoded for auto calibration and quality assurance. Most significantly, towards the end of this decade, the first enzyme electrode strips were introduced.

Lifescan introduced Glucoscan II and Glucoscan 2000 in 1983 and 1986, respectively, with improved meter reliability. However, assessments of the ease of use and analytical performance by laboratory and nursing staff using Glucoscan 2000 were generally inconsistent and disappointing.[12,13]The aptly named OneTouch meter was introduced in 1987 and was regarded as a 'second generation' blood glucose monitoring system (BGMS) because it utilized a modified sampling procedure.

In 1982, Boehringer Mannheim (BM) launched Reflocheck, a small portable reflectance meter using Reflotest strips which were wiped with a cotton ball and hada barcode for calibration. Evaluations showed excellent correlation and good precision, and results from a diabetes screening study in general practice demonstrated cost benefits. In 1984, BM marketed the first of a series of Accu-Chek (Reflolux in Europe) meters, which used improved reagent strips that required smaller volumes of blood, including BM Test-Glycemie 20-800R that could also be read visually with a more stable colour. In 1986, Accu-Chek II became available and received good performance reports in comparison with other equivalent BGMS. [14, 15]

IV. EMERGENCE OF SMALLER METERS: 1991–2000

Glucose became one of the most frequently measured analyses in clinical units, primary care and by patients for monitoring at home, made possible through the availability of systems based on dry-reagent test strips with visually read end-points and/or simple-to-use reflectance meters and biosensors. However, the first-generation blood glucose systems had a number of operator-dependent steps, with the possibility of obtaining misleading results adversely affecting patient treatment. These were highlighted in a number of publications at the time and led to the Department of Health issuing a Hazard Notice. [17]These difficulties were mainly in obtaining a sufficient volume of blood, inaccuracies in timing the application and removal of blood from the test strip, inaccurate wiping technique, calibration/coding errors, lack of maintenance and quality control procedures. In light of these concerns, many manufacturers went on to develop systems that eliminated or minimized these operator-dependent steps.

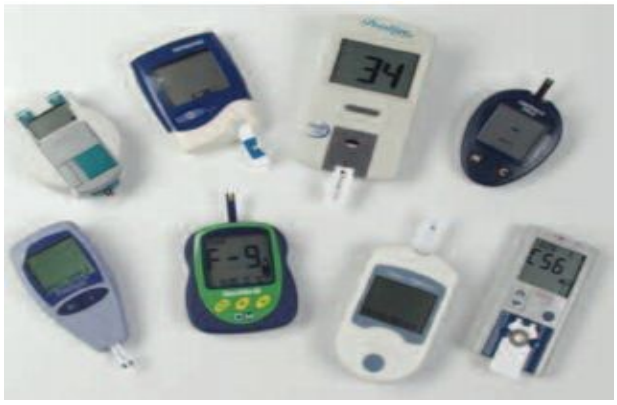

Fig. 2: With the 21st century came a number of different electrochemical glucose meter systems, including the OneTouch Ultra (top right) from Johnson & Johnson.

V. THE RISE OF NONINVASIVE OPTICAL GLUCOSE MONITORING SYSTEM

Noninvasive glucose refers to the measurement of blood glucose levels without drawing blood, puncturing the skin, or causing pain or trauma. The search for a successful technique began about 1975 and has continued to the present without a clinically or commercially viable product.[17-18]Approaches that have been tried include near infrared spectroscopy (measuring glucose through the skin using light of slightly longer wavelengths than the visible region),[19] transdermal measurement (attempting to pull glucose through the skin using either chemicals, electricity or ultrasound), measuring the amount that polarized light is rotated by glucose in the front chamber of the eye (containing the "aqueous humor"), and many others.

Non-invasive optical measurement of glucose is performed by focusing a beam of light onto the body. The light is modified by the tissue after transmission through the target area. An optical signature or fingerprint of the tissue content is produced by the diffuse light that escapes the tissue it has penetrated. The absorbance of light by the skin is due to its chemical components (i.e., water, hemoglobin, melanin, fat and glucose). The transmission of light at each wavelength is a function of thickness, color and structure of the skin, bone, blood and other material through which the light passes [20].

The glucose concentration can be determined by analyzing the optical signal changes in wavelength, polarization or intensity of light. The sample volume measured by these methods depends on the measurement site. The correlation with blood glucose is based on the percent of fluid sample that is interstitial, intracellular or capillary blood. Drs. Roe and Smoller [20] have devised the following example. The fluid viewed through the limb is 63% intracellular and 37% extracellular, of which 27% is interstitial and 10% plasma. A blood glucose value of 100mg/dl is equivalent to a tissue sample glucose average of 38mg/dl of which 26% is due to blood, 58% is due to interstitial fluid and 16% is due to intracellular fluid. What the tissue sample glucose means clinically in respect, to therapy is still under investigation.

Not only is the optical measurement dependent on concentration changes in all body compartments measured, but changes in the ratio of tissue fluids (as altered by activity level, diet or hormone fluctuations) and this, in turn, effects the glucose measurement. Problems also occur due to changes in the tissue after the original calibration and the lack of transferability of calibration from one part of the body to another. Tissue changes include: body fluid source of the blood supply for the body fluid being measured, medications that affect the ratio of tissue fluids, day-to-day changes in the vasculature, the aging process, diseases and the person‘s metabolic activity.

VI. CONCLUSION

It is evident that great progress has been made during the past 40 years and, although here are slight variations, the modern blood glucose meter has evolved into an almost standard size and shape. These are battery powered, handheld, and easy to use and contain advanced micro-electronics, optical techniques and software to perform a range of useful functions.

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